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19 ENGEL JUTTA/AU

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12 REISSMANN CARLOS BRUNO/AU

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                OR "REISSMAN THOMAS LINCOLN"/AU)
=> s 11-14
            261 (L1 OR L2 OR L3 OR L4)
=> s 15 and cetrorelix
             29 L5 AND CETRORELIX
=> dup rem 16
PROCESSING COMPLETED FOR L6
              22 DUP REM L6 (7 DUPLICATES REMOVED)
=> d bib ab 1-22
L7
     ANSWER 1 OF 22 USPATFULL
AN
       2001:173567 USPATFULL
TI
       Means for treating prostate hypertrophy and prostate cancer
       Engel, Jurgen, Alzenau, Germany, Federal Republic of
IN
       Reissmann, Thomas, Frankfurt am Main, Germany, Federal
Republic of
       Riethmuller-Winzen, Hilde, Frankfurt am Main, Germany, Federal
Republic
       Rawert, Jurgen, Alzenau, Germany, Federal Republic of
       ASTA Medica Aktiengesellschaft, Dresden, Germany, Federal
Republic of
        (non-U.S. corporation)
PΙ
       US 6300313
                     B1
                                  20011009
ΑI
       US 1999-401851
                                  19990922 (9)
RLI
       Division of Ser. No. US 1998-57458, filed on 9 Apr 1998, now
patented,
       Pat. No. US 5998377
PRAI
       US 1996-25990
                              19960912 (60)
       US 1997-43228
                              19970410 (60)
DT
       Utility
FS
       GRANTED
EXNAM Primary Examiner: Goldberg, Jerome D.
       Pillsbury Winthrop LLP
CLMN
       Number of Claims: 5
ECL
       Exemplary Claim: 1
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DRWN 7 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 258
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A regime for therapeutic management of a benign prostatic hyperplasia
and prostatic cancer employs Cetrorelix alone or in combination with .alpha.-reductase inhibitors or .alpha.-receptor

.alpha.-receptor
blocking agents. The regiment reduces the volume of the prostate and

avoids the side effects associated with testosterone levels being in a

castration range. **Cetrorelix** is administered at dosages between 0.5 mg/day and 20 mg/week or about 0.014 mg/kg body weight per

day to 0.30 mg/kg body weight per week or at levels of about 25 to 120

mg of **Cetrorelix** per month or 0.376 mg/kg to 1.71 mg/kg per month. **Cetrorelix** can be administered with .alpha.-reductase inhibitors or a .alpha.-receptor blocking agents.

L7 ANSWER 2 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1

AN 2001:192045 BIOSIS

DN PREV200100192045

TI Diagnostic composition containing an LH-RH antagonist for hysteroscopy.

AU Engel, Jurgen (1); Diedrich, Klaus; Felberbaum, Ricardo

CS (1) Alzenau Germany

ASSIGNEE: Asta Medica Aktiengesellschaft, Germany

PI US 6106805 August 22, 2000

SO Official Gazette of the United States Patent and Trademark Office Patents,

(Aug. 22, 2000) Vol. 1237, No. 4, pp. No Pagination. e-file. ISSN: 0098-1133.

DT Patent

LA English

AB The invention relates to a diagnostic composition for improving the

effectiveness of hysteroscopy, characterized in that it contains an LH-RH

antagonist, in particular **cetrorelix**. The composition is envisaged for use prior to hysteroscopy and/or for preparation for

surgery, specifically in a single dose of between 0.1 and 2 mg/kg.

However, the composition can also be administered, for use prior to

hysteroscopy and/or for preparation for surgery, in a multiple dose of

between 0.01 and 0.5 mg/kg, preferably spread over 1-14 days. The composition is furthermore suitable for use in hysteroscopy in combination

with the subsequent treatment of pathological conditions of the uterus

such as myoma and endometrial hyperplasia.

L7 ANSWER 3 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2

AN 2000:477618 BIOSIS

DN PREV200000477618

TI Process for the preparation of immobilized and activity-stabilized

complexes of LHRH antagonists.

- AU Engel, Jurgen (1); Deger, Wolfgang; Reissmann, Thomas; Losse, Gunter; Naumann, Wolfgang; Murgas, Sandra
- CS (1) Alzenau Germany

ASSIGNEE: Asta Medica Aktiengesellschaft, Dresden, Germany

PI US 6054555 April 25, 2000

SO Official Gazette of the United States Patent and Trademark Office Patents,

(Apr. 25, 2000) Vol. 1233, No. 4, pp. No pagination. e-file. ISSN: 0098-1133.

DT Patent

LA English

AB In this invention, a release-delaying system is to be developed for LHRH

antagonists, in particular for **cetrorelix**, which allows the active compound to be released in a controlled manner over several weeks

by complexation with suitable biophilic carriers. The acidic polyamino

acids polyglutamic acid and polyaspartic acid were selected for complexation with **cetrorelix**. The **cetrorelix** polyamino acid complexes are prepared from aqueous solutions by

combination of the

solutions and precipitation of the complexes, which are subsequently

centrifuged off and dried over P2 O5 in vacuo. If complexes having a

defined composition are to be obtained, lyophilization proves to be a

suitable method. The **cetrorelix**-carboxylic acid complexes were also prepared from the aqueous solutions. In the random liberation system,

the acidic polyamino acids poly-Glu and poly-Asp showed good release-delaying properties as a function of the hydrophobicity and the

molecular mass of the polyamino acid. In animal experiments, it was

possible to confirm the activity of the **cetrorelix**-polyamino acid complexes as a depot system in principle. It is thus possible by

complexation of **cetrorelix** with polyamino acids to achieve testosterone suppression in male rats over 600 hours. The celease of

active compound here can be controlled by the nature and the molecular

mass of the polymers.

- L7 ANSWER 4 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
- AN 2000:484741 BIOSIS
- DN PREV200000484741
- TI Means for treating prostate hypertrophy and prostate cancer.
- AU Engel, Jurgen (1); Reissmann, Thomas; Riethmuller-Winzen, Hilde; Rawert, Jurgen
- CS (1) Alzenau Germany

ASSIGNEE: Asta Medica Aktiengesellschaft, Germany

- PI US 6054432 April 25, 2000
- ${\tt SO}$  Official Gazette of the United States Patent and Trademark Office Patents,

(Apr. 25, 2000) Vol. 1233, No. 4, pp. No pagination. e-file. ISSN: 0098-1133.

DT Patent

LA English

AB A regime for therapeutic management of a benign prostatic hyperplasia and

prostatic cancer employs **Cetrorelix** alone or in combination with alpha-reductase inhibitors or alpha-receptor blocking agents. The regimen

reduces the volume of the prostate and avoids the side effects associated

with testosterone levels being in a castration range **Cetrorelix** is administered at dosages between 0,5 mg/day and 20 mg/week or about

0.014 mg/kg body weight per day to 0,30 mg/kg body weight per week or at

levels of about 25 to 120 mg of **Cetrorelix** per month or 0.376 mg kg to 1.71 mg/kg per month **Cetrorelix** can be administered with alpha-reductase inhibitors or alpha-receptor blocking agents.

L7 ANSWER 5 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4

AN 2000:355483 BIOSIS

DN PREV200000355483

TI Immobilized and activity-stabilized complexes of LHRH antagonists and

processes for their preparation.

AU Engel, Jurgen (1); Deger, Wolfgang; Reissmann, Thomas; Losse, Gunter; Naumann, Wolfgang; Murgas, Sandr

CS (1) Alzenau Germany

ASSIGNEE: Asta Medica Aktiengesellschaft, Dresden, Germany

PI US 6022860 February 08, 2000

SO Official Gazette of the United States Patent and Trademark Office Patents,

(Feb. 8, 2000) Vol. 1231, No. 2, pp. No pagination. e-file. ISSN: 0098-1133.

DT Patent

LA English

AB In this invention, a release-delaying system is to be developed for LHRH

antagonists, in particular for **cetrorelix**, which allows the active compound to be released in a controlled manner over several weeks

by complexation with suitable biophilic carriers. The acidic polyamino

acids polyglutamic acid and polyaspartic acid were selected for complexation with **cetrorelix**. The **cetrorelix** polyamino acid complexes are prepared from aqueous solutions by

combination of the

solutions and precipitation of the complexes, which are subsequently

centrifuged off and dried over P2 05 in vacuo. If complexes having a  $\,$ 

defined composition are to be obtained, lyophilization proves to be a

suitable method. The **cetrorelix**-carboxylic acid complexes were also prepared from the aqueous solutions. In the random liberation system,

the acidic polyamino acids poly-Glu and poly-Asp showed good release-delaying properties as a function of the hydrophobicity and the

molecular mass of the polyamino acid. In animal experiments, it was possible to confirm the activity of the cetrorelix-polyamino acid complexes as a depot system in principle. It is thus possible by complexation of cetrorelix with polyamino acids to achieve testosterone suppression in male rats over 600 hours. The release of active compound here can be controlled by the nature and the molecular mass of the polymers. L7 ANSWER 6 OF 22 USPATFULL AN 2000:70812 USPATFULL Means for treating prostate hypertrophy and prostate cancer ΤI IN Engel, Jurgen, Alzenau, Germany, Federal Republic of Reissmann, Thomas, Frankfurt am Main, Germany, Federal Republic of Riethmuller-Winzen, Hilde, Frankfurt am Main, Germany, Federal Republic of Rawert, Jurgen, Alzenau, Germany, Federal Republic of ASTA Medica AG, Dresden, Germany, Federal Republic of (non-U.S. PA corporation) ΡI US 6071882 20000606 ΑI US 1998-62704 19980420 (9) RLI Division of Ser. No. US 1997-908198, filed on 7 Aug 1997 PRAI US 1996-25990 19960912 (60) US 1997-43228 19970410 (60) DTUtility FS Granted EXNAM Primary Examiner: Goldberg, Jerome D. LREP Pillsbury Madison & Sutro LLP Number of Claims: 12 CLMN ECL Exemplary Claim: 1 DRWN 4 Drawing Figure(s); 4 Drawing Page(s) LN.CNT 273 CAS INDEXING IS AVAILABLE FOR THIS PATENT. A regime for therapeutic management of a benign prostatic AB hyperplasia and prostatic cancer employs Cetrorelix alone or in combination with .alpha.-reductase inhibitors or .alpha.-receptor blocking agents. The regimen reduces the volume of the prostate and avoids the side effects associated with testosterone levels castration range. Cetrorelix is administered at dosages between 0.5 mg/day and 20 mg/week or about 0.014 mg/kg body weight per day to 0.30 mg/kg body weight per week or at levels of about 25 to 120 mg of Cetrorelix per month or 0.376 mg/kg to 1.71 mg/kg per month. Cetrorelix can be administered with .alpha.-reductase inhibitors or .alpha.-receptor blocking agents. L7

L7 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2001 ACS AN 2000:725497 CAPLUS

DN 133:261948

```
Method for a programmed controlled ovarian stimulation protocol
ΤI
     Engel, Jurgen; Riethmuller-winzen, Hilde
IN
     Asta Medica A.-G., Germany
PA
     PCT Int. Appl., 17 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LΆ
     English
FAN.CNT 1
                                         APPLICATION NO. DATE
     PATENT NO.
                     KIND DATE
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                                           -----
                            20001012
                                           WO 2000-EP2466
                                                            20000321
ΡI
     WO 2000059542
                      Α1
        W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN,
IS, JP,
             KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI,
SK, TR,
             UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL,
             PT, SE
PRAI US 1999-127241
                       Ρ
                            19990331
     US 1999-131632
                       Ρ
                            19990428
     A method of therapeutic management of infertility by programming
AΒ
of
     controlled ovarian stimulation (COS) and assisted reproductive
procedures
     (ART) the improvement consisting of (a) suppression of premature
ovulation
     with an LHRH-antagonist in controlled ovarian stimulation (COS)
and
     assisted reproductive techniques (ART) with multiple follicle
and oocyte
     development; (b) programming the start of controlled ovarian
stimulation
     (COS) by the administration of progestogen only - or
alternatively
     combined oral contraceptive prepns.; (c) exogenous stimulation
     ovarian follicle growth; (d) ovulation induction with HCG,
native LHRH,
     LHRH-agonists or recombinant LH; (e) application of assisted
reprodn.
     techniques, esp. of IVF, ICSI, GIFT, ZIFT or by intrauterine
insemination
    by sperm injection.
RE.CNT 6
(1) Albano, C; HUMAN REPRODUCTION 1996, V11/10(2114-2118)
(2) Asta Medica Ag; EP 0788799 A 1997 CAPLUS
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- (3) Asta Medica Ag; CA 2200541 A 1998 CAPLUS
- (4) Bouchard, P; OVULATION INDUCTION: UPDATE: THE PROCEEDINGS OF THE WORLDCONGRESS ON OVULATION INDUCTION 1998, P115 CAPLUS
- (5) Felberbaum, R; IN VITRO FERT ASSISTED REPROD, PROC WORLD CONGR 1997, P397

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2001 ACS AN 2000:894792 CAPLUS

DN 134:141823

New LHRH antagonists with enhanced biological activity: Preclinical and clinical results Kutscher, Bernhard; Bernd, Michael; Gunther, Eckhard; Deger, ΑU Wolfgang; Reissmann, Thomas; Beckers, Thomas; Deghenghi, Romano; Engel, Jurgen Corporate Research, ASTA Medica AG, Frankfurt, D-60314, Germany CS Pept. New Millennium, Proc. Am. Pept. Symp., 16th (2000), Meeting Date 1999, 655-657. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Publisher: Kluwer Academic Publishers, Dordrecht, Neth. CODEN: 69ATHX DTConference; General Review LΑ English A brief review/discussion with 4 refs. on the title topic with AΒ focus on Cetrorelix, Antarelix, and D-26344 and their use in treating sex hormone-dependent tumors and nonmalignant conditions. RE.CNT 4 RE (1) Bernd, M; PCT/DE96/02171 (2) Deghenghi, R; WO 92/19651 A1 CAPLUS (3) Kutscher, B; Angew Chem 1997, V109, P2240 (4) Muller, A; Int J Peptide Protein Res 1994, V43, P264 MEDLINE ANSWER 9 OF 22 CAPLUS COPYRIGHT 2001 ACS L7AN 2000:26845 CAPLUS DN132:160805 ΤI Disposition and metabolism of cetrorelix, a potent luteinizing hormone-releasing hormone antagonist, in rats and dogs Schwahn, Martin; Schupke, Hubert; Gasparic, Antje; Krone, ΑU Dorothee; Peter, Gernot; Hempel, Roland; Kronbach, Thomas; Locher, Mathias; Jahn, Wolfgang; Engel, Jurgen Corporate Research and Development, ASTA Medica AG, CS Frankfurt/Main, D-60314, Germany SO Drug Metab. Dispos. (2000), 28(1), 10-20 CODEN: DMDSAI; ISSN: 0090-9556 American Society for Pharmacology and Experimental Therapeutics PΒ DT Journal LΑ English Disposition and metab. of cetrorelix was studied in intact and bile duct-cannulated rats and dogs after s.c. injection. An s.c. dose of 0.1 mg/kg [14C]cetrorelix was rapidly and completely absorbed in rats. Tmax in plasma and most tissues was at 2 h. Radioactivity at the injection site in rats declined to 10% by 24 h. The extent of 14C absorption in rats calcd. from excretion until 264 h was 94%. Exposure of the target organ pituitary gland was demonstrated with a time course similar to plasma but on a higher level. Rats excreted 69.6% of radioactivity via feces and 24.3% into urine. Excretion was nearly

complete within 48 h. No enteral resorption was detected. In dogs tmax

in plasma was 1.3 h. 14C- and cetrorelix plasma levels were similar until 24 h, indicating a negligible amt. of metabolites.

of 1 mg/kg in dogs showed an increasing influence of a slow absorption

phase (flip-flop). In dogs equal amts. of the 14C dose were found within

192 h in feces and urine, 46 and 48%, resp. In urine of both species,

only intact cetrorelix was detected. In bile and feces of both species qual. the same metabolites were found, characterized as truncated

peptides of the parent decapeptide. The major metabolite occurring in

bile of both species was the (1-7)heptapeptide. The amts. of the (1-4)tetrapeptide in feces of rats but not in that of dogs increase with

time, suggesting addnl. degrdn. of the peptide in the gastrointestinal

tract of rats by enteric metabolization.

RE.CNT 24

RE

- (2) Bajusz, S; Proc Natl Acad Sci USA 1988, V85, P1637 CAPLUS
- (5) Berger, H; Drug Metab Dispos 1993, V21, P818 CAPLUS
- (6) Berger, H; Regul Pept 1991, V33, P299 CAPLUS
- (7) Chan, R; Biochem Biophys Res Commun 1985, V127, P673 CAPLUS
- (8) Chan, R; Drug Metab Dispos 1991, V19, P858 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L7 ANSWER 10 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5
- AN 2000:292181 BIOSIS
- DN PREV200000292181
- TI Means for treating prostate cancer.
- AU Engel, Jurgen; Reissmann, Thomas (1); Riethmuller-Winzen, Hilde; Rawert, Jurgen
- CS (1) Frankfurt/Main Germany

ASSIGNEE: ASTA Medica Aktiengesellschaft

- PI US 5998377 December 07, 1999
- ${\tt SO}$   ${\tt Official}$  Gazette of the United States Patent and Trademark Office Patents,

(Dec. 7, 1999) Vol. 1229, No. 1, pp. No pagination. e-file.. ISSN: 0098-1133.

DT Patent

LA English

AB A regime for therapeutic management of a benign prostatic hyperplasia and

prostatic cancer employs **Cetrorelix** alone or in combination with alpha-reductase inhibitors or alpha-receptor blocking agents. The regimen

reduces the volume of the prostate and avoids the side effects associated

with testosterone levels being in a castration range. **Cetrorelix** is administered at dosages between 0,5 mg/day and 20 mg/week or about

0.014 mg/kg body weight per day to 0,30 mg/kg body weight per week or at  $\,$ 

levels of about 25 to 120 mg of Cetrorelix per month or 0.376

mg/kg to 1.71 mg/kg per month. Cetrorelix can be administered with alpha-reductase inhibitors or alpha-receptor blocking agents. L7 ANSWER 11 OF 22 USPATFULL AN 1999:146533 USPATFULL TI Nova- and decapeptides in the preparation of a drug for the treatment of aids IN Engel, Jurgen, Alzenau, Germany, Federal Republic of Kutscher, Bernhard, Maintal, Germany, Federal Republic of Bernd, Michael, Frankfurt am Main, Germany, Federal Republic of Niemeyer, Ulf, Offenbach, Germany, Federal Republic of ASTA Medica AG, Germany, Federal Republic of (non-U.S. PA corporation) US 5985834 PΙ 19991116 WO 9500168 19950105 ΑI US 1995-569111 19951218 (8) WO 1994-EP1037 19940402 19951218 PCT 371 date 19951218 PCT 102(e) date DE 1993-4320201 PRAI 19930618 DT Utility FS Granted EXNAM Primary Examiner: Tsang, Cecilla J.; Assistant Examiner: Delacroix-Muirheid, C. LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro  $_{
m LLP}$ CLMN Number of Claims: 24 ECLExemplary Claim: 1 DRWN No Drawings LN.CNT 424 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Described are LHRH-antagonistic and bombesin-antagonistic nona- and decapeptides suitable for use in the preparation of a drug for the treatment of AIDS and ARC as well as for use in the preparation of an immunostimulation drug. L7ANSWER 12 OF 22 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD AN 1999-542841 [46] WPIDS CR 1994-265229 [33] DNC C1999-158621 Treatment of female infertility, especially by in-vitro fertilization. DC B04 IN ENGEL, J; REISSMANN, T; SAUERBIER, D; WICHERT, B (ASTA) ASTA MEDICA AG PACYC 17 PΙ EP 947200 A2 19991006 (199946)\* DE R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE ADT EP 947200 A2 Div ex EP 1994-101672 19940204, EP 1999-102340

NOVELTY - Sterile freeze-dried cetrorelix acetate (a peptide

19940204

FDT EP 947200 A2 Div ex EP 611572 PRAI DE 1993-4305225 19930219

947200 A UPAB: 19991110

described in EP299402) is used in the treatment of female infertility.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the

following: (1) use of sterile freeze-dried cetrorelix acetate for protecting gonads against noxious agents that damage germ cells, e.g.

radiation treatment and chemotherapy; (2) a composition comprising sterile

freeze-dried cetrorelix acetate and optionally excipients for use in the treatment of female infertility; (3) a composition comprising

sterile freeze-dried cetrorelix acetate and optionally excipients for protecting gonads against noxious agents that

cells, e.g. radiation treatment and chemotherapy with cytostatic

ACTIVITY - None given.

MECHANISM OF ACTION - Luteinizing hormone-releasing hormone (LHRH)

antagonist.

USE - In an in-vitro fertilization procedure in which cetrorelix is administered to control the time of ovulation during

an ovary stimulation treatment by preventing a pre-ovulation increase in

luteinizing hormone (LH) levels, whereupon exogenous gonadotropin is

administered to induce ovulation after follicle maturation. Dwg.0/0

ANSWER 13 OF 22 CAPLUS COPYRIGHT 2001 ACS L7

AN 1999:708625 CAPLUS

DN131:295922

Method for the treatment of fertility disorders using an LHRH TI

to partially suppress endogenous gonadotropins during intrauterine

insemination

Engel, Jurgen; Riethmuller-Winzen, Hilde; Reissmann, Thomas IN

PΑ Asta Medica Aktiengesellschaft, Germany

SO PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DT Patent

English LΑ

FAN.CNT 1

	PAT	rent :	NO.		KII	ND	DATE			A.	PPLI	CATI	ON NO	٥.	DATE	
										_						
PΙ	WO	9955	357		A:	1	1999	1104		W	O 19	99-E	P213	3	1999	0329
		W:	AU,	BG,	BR,	BY,	CA,	CN,	CZ,	EE,	GE,	HR,	HU,	ID,	IL,	IN,
IS,	JP,															
			KG,	KR,	ΚŻ,	LT,	LV,	MK,	MX,	NO,	NZ,	PL,	RO,	RU,	SG,	SI,
SK,	TR,															
			UA,	UZ,	YU,	ZA,	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM	
		RW:	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,
MC,	NL,						·	-	-	-	-		-	•	•	•
·	•		PT.	SE												

AU 9937028 AU 1999-37028 A1 19991116 19990329 BR 9909802 A 20001226 BR 1999-9802 19990329 EP 1082129 A1 20010314 EP 1999-919152 19990329 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO

NO 2000005145 A 20001013 NO 2000-5145 20001013

PRAI US 1998-82743 P 19980423 WO 1999-EP2133 W 19990329

B In the method of therapeutic management of infertility by

insemination the improvement consisting of (a) the dose-dependent suppression of endogenous gonadotropins, esp. LH, with a LH-RH Antagonist

allowing the maintenance of physiol. estrogen levels, (b) exogenous

stimulation of the ovarian follicle growth, (c) ovulation induction with

HCG, native LHRH, LHRH-Agonists or recombinant LH, (d) intrauterine

insemination by sperm injection. The LHRH Antagonists may be preferably

Cetrorelix or Antarelix. The stimulation is performed by administration of HMG or recombinant FSH with or without recombinant LH or

with antiestrogens as for example Chlomiphene as well as with the combination of antiestrogens as for example Chlomiphene with gonadotropins.

RE.CNT 5

intrauterine

RE

- (1) Asta Medica AG; EP 0611572 A 1994 CAPLUS
- (2) Asta Medica AG; EP 0788799 A 1997 CAPLUS
- (3) Bouchard, P; Ovul Ind Update '98, Proc World Conf, 2nd 1998, P115 CAPLUS
- (4) Crowley, W; US 5130137 A 1992 CAPLUS
- (5) Schering AG; DE 19604231 A 1997 CAPLUS
- L7 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2001 ACS
- AN 2000:739102 CAPLUS
- DN 134:275789
- TI Development of the LH-RH antagonist Cetrorelix for tumor therapy
- AU Perrissoud, Daniel; Reissmann, Thomas; Engel, Jurgen
- CS Corporate Research & Development ASTA Medica, Frankfurt,

D-60314, Germany

- SO Actual. Chim. Ther. (1999), 25, 243-249 CODEN: ACHTD9; ISSN: 0338-8999
- PB Editions Scientifiques et Medicales Elsevier
- DT Journal; General Review
- LA English
- AB A review with 10 refs. The availability of the LH-releasing hormone-antagonist Cetrorelix for clin. use opens up new therapeutic modalities of diseases dependent on sex hormones.

  RE.CNT 10

RE

- (1) Bajusz, S; Proc Natl Acad Sci 1988, V85, P1637 CAPLUS
- (2) Behre, H; Exp and Clin Endocrinol 1994, V40, P241 CAPLUS
- (6) Matsuo, H; Biochem Biophys Res Commun 1971, V43, P1334 CAPLUS
- (7) Reissmann, T; Eur J Cancer 1996, V32A, P1574 CAPLUS
- (8) Reissmann, T; Hum Reprod 1995, V10, P1974 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L7
    ANSWER 15 OF 22 USPATFULL
                                                     DUPLICATE 6
      1998:75185 USPATFULL
AN
TI
      Long-acting injection suspensions and a process for their
preparation
ΙN
      Engel, Jurgen, Alzenau, Germany, Federal Republic of
      Klokkers-Bethke, Karin, Lenggries, Germany, Federal Republic of
      Reissman, Thomas, Frankfurt, Germany, Federal Republic of
      Hilgard, Peter, Frankfurt, Germany, Federal Republic of
      Asta Medica Aktiengellschaft, Dresden, Germany, Federal
PA
Republic of
      (non-U.S. corporation)
PΙ
      US 5773032
                             19980630
ΑI
      US 1996-661017
                             19960610 (8)
DT
      Utility
FS
      Granted
EXNAM
      Primary Examiner: Azpuru, Carlos A.
      Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro
LREP
LLP
CLMN
      Number of Claims: 8
ECL
      Exemplary Claim: 1
DRWN
      4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 373
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      Poorly soluble salts of LHRH analogues, for example cetrorelix
AΒ
      embonate, display an intrinsic sustained release effect in the
grain
      size 5 .mu.m to 200 .mu.m.
L7
    ANSWER 16 OF 22 CAPLUS COPYRIGHT 2001 ACS
ΑN
    1998:180776 CAPLUS
DN
    128:226267
TI
    Means for treating prostate hypertrophy and prostate cancer with
    Cetrorelix, alone or in combination with other agents
IN
    Engel, Jurgen; Reissmann, Thomas; Riethmuller-Winzen, Hilde;
    Rawert, Jurgen
PA
    Asta Medica A.-G., Germany
    PCT Int. Appl., 25 pp.
SO
    CODEN: PIXXD2
DT
    Patent
LΑ
    English
FAN.CNT 1
    PATENT NO. KIND DATE
                                       APPLICATION NO. DATE
    -----
                                       -----
    WO 9810781 A1 19980319
PΙ
                                       WO 1997-EP4740 19970901
        W: AU, BR, CN, CZ, EE, HU, IL, IS, JP, KR, LT, LV, MX, NO,
NZ, PL,
            RO, RU, SG, SI, SK, TR, UA
        RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
NL, PT, SE
    US 6054432
                          20000425
                     Α
                                        US 1997-908198
                                                         19970807
    AU 9746198
                     A1
                          19980402
                                        AU 1997-46198
                                                         19970901
    EP 925069
                     A1
                          19990630
                                        EP 1997-944818
                                                        19970901
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
            IE, SI, LT, LV, FI, RO
    CN 1230121
                   A 19990929
                                        CN 1997-197904 19970901
    BR 9713197
                    Α
                         20000404
                                       BR 1997-13197 19970901
                    T2 20010116
    JP 2001500500
                                       JP 1998-513204 19970901
               AA 19980312
                                   CA 1997-2215015 19970910
    CA 2215015
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	***	E0000==	70	10001007	***	1000 55450	10000400
	US	5998377	A	19991207	US	1998-57458	19980409
	US	6071882	Α	20000606	US	1998-62704	19980420
	NO	9901192	Α	19990428	NO	1999-1192	19990311
	US	6300313	B1	20011009	US	1999-401851	19990922
PRAI	US	1996-25990	P	19960912			
	US	1997-43228	P	19970410			
	US	1997-908198	A3	19970807			
	WO	1997-EP4740	W	19970901			
	US	1998-57458	A3	19980409			
					_	and the second s	

AB A regime for therapeutic management of a benign prostatic hyperplasia and

prostatic cancer employs **Cetrorelix** alone or in combination with .alpha.-reductase inhibitors or .alpha.-receptor blocking agents. The

regimen reduces the vol. of the prostate and avoids the side effects

assocd. with testosterone levels being in a castration range.

Cetrorelix is administered at dosages between 0.5 mg/day and 20 mg/wk or about 0.014 mg/kg body wt. per day to 0.30 mg/kg body wt. per wk

or at levels of about 25 to 120 mg of **Cetrorelix** per mo or 0.376 mg/kg to 1.71 mg/kg per mo. **Cetrorelix** can be administered with .alpha.-reductase inhibitors or .alpha.-receptor blocking agents.

- L7 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2001 ACS
- AN 1999:538778 CAPLUS
- DN 131:139954
- TI LHRH antagonists in the treatment of fertility disorders
- IN Bouchard, Philippe; Frydman, Rene; Diedrich, Klaus; Engel, Jurgen; Devroey, Paul
- PA Asta Medica AG, Germany
- SO Can. Pat. Appl., 15 pp. CODEN: CPXXEB
- D. D.
- DT Patent LA English
- FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO,	DATE	
			<b></b>			
PI	CA 2200541	AA	19980722	CA 1997-2200541	19970320	
PRAT	US 1997-786937		19970122			

AB A method of treating infertility disorders by administering an LH-RH

antagonist, preferably **Cetrorelix**, in amts. to selectively suppress endogenous LH but not FSH secretion and inducing follicle growth

by administration of exogenous gonadotropin. The selective suppression of

LH allows FSH secretion to be at natural levels thereby not affecting

individual estrogen development. The LH-RH antagonist can be given as a

single or dual s.c. dose in the range of 1 mg to 10 mg,
preferably 2 mg -

- 6 mg. In multiple dosing posol., LH-RH antagonist can be administered
- s.c. in an amt. in the range of 0.1 to 0.5 mg of LH-RH antagonist/day.

LH-RH antagonist is applied starting cycle day 1 to 10, preferably on day

4 to 8, and ovulation can be induced between day 9 and 20 of the menstruation cycle by administering rec. LH, native LH-RH, LH-RH agonist or by HCG. In addn. rec. LH, native LH-RH or LH-RH agonist can be given to avoid hyperstimulation syndrome and native LH-RH or a LH-RH agonist can be administered to avoid luteal phase stimulation by neutralizing the neg. effects of HCG. L7 ANSWER 18 OF 22 USPATFULL AN 97:78416 USPATFULL TIProducts for administering an initial high dose of Cetrorelix and producing a combination package for use when treating diseases IN Engel, Jurgen, Alzenau, Germany, Federal Republic of Hilgard, Peter, Frankfurt, Germany, Federal Republic of Reissmann, Thomas, Frankfurt, Germany, Federal Republic of PΑ ASTA Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of (non-U.S. corporation) PΙ US 5663145 19970902 US 1994-354838 ΑI 19941208 (8) DE 1993-4342091 19931209 PRAI DT Utility FS Granted EXNAM Primary Examiner: Russel, Jeffrey E. LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLPCLMN Number of Claims: 25 ECLExemplary Claim: 7 DRWN No Drawings LN.CNT 227 CAS INDEXING IS AVAILABLE FOR THIS PATENT. For application during the treatment of benign and malign tumour diseases, the product according to the invention containing the initial dose of Cetrorelix acetate and one or more maintenance doses of Cetrorelix acetate, Cetrorelix embonate or a slow-release form of Cetrorelix, is used as a combination preparation for treatment to be administered at specific time intervals. L7 ANSWER 19 OF 22 USPATFULL AN 95:43015 USPATFULL TICompressed gas packages using polyoxyethylene glyceryl oleates IN Hettche, Helmut, Dietzenbach, Germany, Federal Republic of Engel, Jurgen, Alzenau, Germany, Federal Republic of Muckenschnabel, Reinhard, Frankfurt, Germany, Federal Republic of Asta Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of (non-U.S. corporation) ΡI US 5415853 19950516 ΑI US 1993-33789 19930317 (8) DE 1992-42085055 19920317 DE 1992-42151880 19920508 PRAI

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DE 1992-42308763 19920916
DT
           Utility
FS
           Granted
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner:
Benston, Jr.,
           William E.
           Cushman Darby & Cushman
LREP
           Number of Claims: 6
CLMN
ECL
           Exemplary Claim: 1
DRWN
           No Drawings
LN.CNT 314
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
           Aerosol compressed gas packages containing a member of the
group
           consisting of polyoxyethylene-25-glyceryl trioleate,
           polyoxyethylene-30-glyceryl monooleate and
polyoxyethylene-20-glyceryl
           monooleate as suspension stabilizer and/or valve lubricant.
These
           materials are especially useful when the package contains TG
227 or TG
           134a as the propellant.
L7
        ANSWER 20 OF 22 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
DUPLICATE
        7
AN
        1994-265229 [33]
                                       WPIDS
DNC C1994-121294
        Freeze-dried peptide compsns. - prepd. by freeze drying soln. of
ΤI
peptide
        in aq. acetic acid.
DC
        B04
        ENGEL, J; REISSMANN, T; SAUERBIER, D; WICHERT, B; BURKHARD, W;
IN
        JUERGEN, E
        (ASTA) ASTA MEDICA AG
PA
CYC 32
ΡI
        EP 611572
                              A2 19940824 (199433)* DE
                                                                              5p
              R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
        DE 4305225 Al 19940825 (199433)
                                                                              5p
       AU 9455235 A 19940825 (199436)

NO 9400564 A 19940822 (199436)

CA 2115943 A 19940820 (199439)

CZ 9400312 A3 19940914 (199439)

BR 9400617 A 19940927 (199440)

SK 9400195 A3 19940907 (199440)

FI 9400779 A 19940820 (199441)

TD 06271476 A 19940827 (199443)
        JP 06271476 A 19940927 (199443)
                                                                              5p

      JP 06271476
      A 19940927 (199443)

      ZA 9401136
      A 19941026 (199444)

      HU 67117
      T 19950228 (199514)

      EP 611572
      A3 19950111 (199538)

      AU 671881
      B 19960912 (199644)

      CN 1112019
      A 19951122 (199737)

      SG 46632
      A1 19980220 (199822)

      BR 1101004
      A3 19980512 (199828)

      CZ 284314
      B6 19981014 (199847)

      NZ 314707
      A 19990225 (199914)

      CZ 285768
      B6 19991117 (200002)

      EP 611572
      B1 20000607 (200032)

                                                                            12p
        EP 611572 B1 20000607 (200032) DE
```

R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

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G 20000713 (200037)
     DE 59409389
                  B 20000728 (200045)
     HU 218281
                 C1 20000210 (200048)
     RU 2145234
                 T3 20001016 (200058)
     ES 2148247
                  A 20000421 (200061)
     TW 387812
ADT EP 611572 A2 EP 1994-101672 19940204; DE 4305225 A1 DE
1993-4305225
     19930219; AU 9455235 A AU 1994-55235 19940217; NO 9400564 A NO
     19940218; CA 2115943 A CA 1994-2115943 19940218; CZ 9400312 A3
CZ 1994-312
     19940214; BR 9400617 A BR 1994-617 19940218; SK 9400195 A3 SK
     19940218; FI 9400779 A FI 1994-779 19940218; JP 06271476 A JP
1994-20532
     19940217; ZA 9401136 A ZA 1994-1136 19940218; HU 67117 T HU
     19940218; EP 611572 A3 EP 1994-101672 19940204; AU 671881 B AU
1994-55235
     19940217; CN 1112019 A CN 1994-101378 19940218; SG 46632 A1 SG
1996-6874
     19940204; BR 1101004 A3 BR 1997-1101004 19970514; CZ 284314 B6
CZ 1994-312
     19940214; NZ 314707 A Div ex NZ 1994-250906 19940217, NZ
1994-314707
     19940217; CZ 285768 B6 CZ 1998-974 19940214; EP 611572 B1 EP
1994-101672
     19940204, Related to EP 1999-102340 19940204; DE 59409389 G DE
1994-509389
     19940204, EP 1994-101672 19940204; HU 218281 B HU 1994-481
19940218; RU
     2145234 C1 RU 1994-5001 19940218; ES 2148247 T3 EP 1994-101672
19940204;
     TW 387812 A TW 1994-100769 19940131
FDT AU 671881 B Previous Publ. AU 9455235; CZ 284314 B6 Previous
Publ. CZ
     9400312; NZ 314707 A Div ex NZ 250906; CZ 285768 B6 Previous
Publ. CZ
     9800974; EP 611572 B1 Related to EP 947200; DE 59409389 G Based
on EP
     611572; HU 218281 B Previous Publ. HU 67117; ES 2148247 T3 Based
on EP
     611572
PRAI DE 1993-4305225 19930219
           611572 A UPAB: 19991110
     Freeze-dried compsns. comprising a peptide of 3-15 amino acid
units and
    opt. one or more matrix materials are characterised in that 1
pt. wt. of
     the peptide is dissolved in 100-10,000 pts. wt. of acetic acid
and then
     transferred to water and the resulting soln. is freeze dried.
         USE/ADVANTAGE - The compsns. esp. contain cetrorelix (EP
     299402), which is used in the treatment of female infertility
(for
    controlling ovulation prior to isolating egg cells for in-vitro
     fertilisation) and for gonad protection in male patients (e.g.
     ratio- or chemotherapy). The aq. acetic acid soln. can be
sterilised by
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Dwg.0/0
     ANSWER 21 OF 22 CAPLUS COPYRIGHT 2001 ACS
L7
AN
     1996:316833 CAPLUS
DN
     125:722
ΤI
     Persistent blockade of the pituitary gonadal axis in patients
with
     prostatic cancer by the LH-RH antagonist SB-75 (Cetrorelix)
AU
    Gonzalez-Barcena, D.; Vadillo-Buenfil, M.; Cortez-Morales, A.;
Romero, M.
     A.; Engel, J.; Comaru-Schally, A. M.; Schally, A. V.; Reissman,
     Th.
CS
     Hosp. Esp. C.M.R., IMSS, Mexico City, Mex.
     Proc. Int. Cancer Congr., Free Pap. Posters, 16th (1994), Volume
SO
3,
     2201-2204. Editor(s): Rao, R. S. Publisher: Monduzzi Editore,
Bologna,
     Italy.
     CODEN: 62UYAO
     Conference
DT
LΑ
     English
AB
     Our objective was to use the LH-RH analog SB-75, Cetrorelix to
     treat a group of patients with advanced prostrate carcinoma.
     antagonists SB-75 was well tolerated. No local or systemic
effects were
            These results show that the chronic administration of the
     obsd.
LH-RH
     antagonists SB-75, Cetrorelix is an effective therapy for the
     management of advanced prostate cancer.
L7
     ANSWER 22 OF 22 CAPLUS COPYRIGHT 2001 ACS
AN
     1995:228423 CAPLUS
DN
     122:106501
TI
     Synthesis of [U-14C] Arg labeled decapeptide cetrorelix, a novel
     luteinizing hormone-releasing hormone antagonist
     Locher, Mathias; Johnston, James; Muller, Thomas; Borbe, Harald
ΑU
0.;
     Kutscher, Bernhard; Engel, Jurgen
CS
    ASTA Medica AG, Frankfurt, D-60001, Germany
SO
     J. Labelled Compd. Radiopharm. (1994), 34(11), 1091-8
     CODEN: JLCRD4; ISSN: 0362-4803
DT
     Journal
     English
LΑ
AΒ
     The decapeptide cetrorelix is a novel LH-releasing hormone
     (LH-RH) antagonist. For nonclin. studies concerning absorption,
     distribution, metab. and excretion (ADME) in animals the
[14C] - labeled
     compd. is essential. Therefore, [U-14C] Arg cetrorelix acetate
     salt was synthesized by Amersham international, Buckinghamshire
(England)
     from precursor peptides provided by Degussa AG, Hanau-Wolfgang
(Germany).
     [U-14C]Arg labeled cetrorelix peptide base has a specific
     activity of 8.13 MBq/mg (220 .mu.Ci/mg) and a mol. wt. of 1442.6
     this specific activity. The chem. and radiochem. purity (92.2%
     decapeptide content and 97.6%, resp.) detd. by HPLC is suitable
for
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filtration without gelation or hydrolysis of the peptide.

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=> e wolf ingrid/au
                   WOLF INGETRAUT/AU
E1
            1
                   WOLF INGO/AU
E2
            15
E3
            40 --> WOLF INGRID/AU
E4
                 WOLF INGRID DE/AU
            1
                   WOLF INGRID H/AU
E5
            3
           1 WOLF IRENE/AU
1 WOLF IRIS/AU
3 WOLF IRMA/AU
8 WOLF IRMELIN/AU
4 WOLF IRVING/AU
17 WOLF IRVING W/AU
2 WOLF IRVING WILLIAM/AU
E6
E7
E8
E9
E10
E11
E12
=> s e3-e5
            44 ("WOLF INGRID"/AU OR "WOLF INGRID DE"/AU OR "WOLF
INGRID H"/AU)
=> s 18 and cetrorelix
            0 L8 AND CETRORELIX
L9
=> s 18 and lyophiliz?
L10
      6 L8 AND LYOPHILIZ?
=> dup rem 110
PROCESSING COMPLETED FOR L10
             6 DUP REM L10 (0 DUPLICATES REMOVED)
=> d bib ab 1-6
L11 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2001 ACS
    1992:46317 CAPLUS
AN
DN
    116:46317
    Preparation of a stable parenteral immunostimulant composition
containing
    splenopentin
IN
    Wolf, Ingrid
PΑ
    Berlin-Chemie A.-G., Germany
SO
    Ger. (East), 3 pp.
    CODEN: GEXXA8
DT
    Patent
LΑ
    German
FAN.CNT 1
                                          APPLICATION NO. DATE
    PATENT NO.
                    KIND DATE
     -----
                                           -----
    DD 292382
PΙ
                      A5
                            19910801
                                          DD 1990-338431 19900306
    DD 292382
                     B5
                          19940324
    EP 445581
                     A1 19910911
                                          EP 1991-102431 19910220
    EP 445581
                      B1 19930505
         R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE
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\mathbf{E}
                            19930515
                                           AT 1991-102431
                                                            19910220
    AT 88903
    ES 2055469
                      Т3
                            19940816
                                           ES 1991-102431
                                                            19910220
                                           CA 1991-2037531 19910304
                      AA
                            19910907
    CA 2037531
                      A2
                            19920803
                                           JP 1991-38808
                                                            19910305
    JP 04211611
    JP 06092315
                      B4
                            19941116
PRAI DD 1990-338431
                            19900306
                            19910220
    EP 1991-102431
```

AB A stable, liq. or **lyophilized** immunostimulant prepn. for parenteral administration to humans contains splenopentin or its analogs

combined with a hydroxybenzoic acid ester as stabilizer. Thus, 27 g

diacetylsplenopentin-HCl was dissolved in 600 mL 0.02M H3PO4; the pH was

adjusted to 8.0-9.0 with NaOH and then adjusted after 20 min to 7.5. Me

hydroxybenzoate 1.5 g was dissolved in 300 mL water at 90-95.degree. and

added to the above soln.; the pH was adjusted to 6.9-7.1 and the soln. was

sterilized by filtration.

L11 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2001 ACS

AN 1989:463948 CAPLUS

DN 111:63948

TI Sustained-release pharmaceuticals containing peptide-sulfonated polystyrene complexes

IN Fechner, Klaus; Bienert, Michael; Klauschenz, Erhard; Wolf,
Ingrid

; Mehlis, Burkhard; Loth, Fritz; Dautzenberg, Horst; Bergfeld, Jost

PA Akademie der Wissenschaften der DDR, Ger. Dem. Rep.

SO Ger. (East), 4 pp.

CODEN: GEXXA8

DT Patent

LA German

ΡI

FAN.CNT 1
PATENT NO. KIND I

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 256605	A3	19880518	DD 1982-246469	19821223

AB Sustained-release pharmaceuticals contain complexes of biol. active

peptides, polypeptides, or their derivs. or salts, with sulfonated

polystyrene or its salts. Polystyrene (mol. wt. 200,000) was sulfonated

and neutralized with NaOH to give a polymer with a degree of substitution

of 1. A **lyophilizate** contg. 2.5 mg angiotensin and 25 mg sorbitol was dissolved in a soln. contg. 0.125% Na polystyrenesulfonate

and isotonic NaCl to give an injection.

L11 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2001 ACS

AN 1981:127390 CAPLUS

DN 94:127390

TI Lyophilized LHRH preparations

IN Wolf, Ingrid; Schneider, Anita; Tschauschev, Peter

PA Ger. Dem. Rep.

```
SO
    Ger. (East), 5 pp.
    CODEN: GEXXA8
DT
    Patent
LA
    German
FAN.CNT 1
                         2A1E
    PATENT NO. KIND DATE
                                       APPLICATION NO. DATE
     -----
                    - - - -
                                        -----
    DD 141996 Z 19800604 DD 1979-211139
                                                         19790221
PΙ
    A stable LH-RH [9034-40-6] prepn. is made by buffering an aq.
AB
soln. of
    LH-RH to pH 3.5-6.5 and lyophilizing. For example, 4.5 g LH-RH,
    to 2 g citric acid [77-92-9] and 20 g mannitol (carrier) were
dissolved
    in 900 mL H2O for injection, dild. to 1 L, and adjusted to pH
3.5-4.5 with
    1N NaOH. The soln. was sterilized by filtration, divided into 1
mL
    aliquots, and lyophilized.
L11 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2001 ACS
AN
    1980:169260 CAPLUS
DN
    92:169260
TI
    Lyophilicized hypotensive preparation for parenteral application
IN
    Wolf, Ingrid; Klehr, Gabriele
PA
    Ger. Dem. Rep.
    Ger. (East), 6 pp.
SO
    CODEN: GEXXA8
DT
    Patent
LA
    German
FAN.CNT 1
    PATENT NO. KIND DATE
                                       APPLICATION NO. DATE
                                        ______
    DD 138406 Z 19791031
DD 138406 B1 19860507
                                       DD 1978-207389 19780821
PΙ
ΑB
    A pharmaceutical prepn. of di-Na pentacyanonitrosylferrate (I)
    [14402-89-2], stable for several y and suitable for parenteral
    application, with I contq. 5-50 mg-% K, was prepd. by adding an
acidic or
    neutral amino acid or a Na salt of a weak acid and(or) mannitol
and
    lyophilizing the soln. Thus, 50 g I contg. 5 mg-% K was
dissolved
    with 20 g mannitol [69-65-8] in 1 L freshly-distd. H2O and the
    sterile-filtered, aseptically filled into 1 mL brown glass
ampuls, and
    lyophilized.
L11 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2001 ACS
AN
    1975:484842 CAPLUS
DN
    83:84842
TI
    Lyophilized gastrin preparations
IN
    Wolf, Ingrid
    E. Ger.
PA
SO
    Ger. (East), 6 pp.
    CODEN: GEXXA8
DT
    Patent
LΑ
    German
```

FAN.CNT 1

```
PATENT NO.
                   KIND DATE
                                        APPLICATION NO. DATE
                                        ______
     -----
                    Z
PΙ
    DD 109512
                         19741112
                                        DD 1974-176286
                                                        19740131
    A parenteral applicable gastrin [9002-76-0] prepn. which is
AΒ
stable at room
    temp. is prepd. by adding trometamol [77-86-1] to a gastrin
soln. and
    lyophilization. A soln. of the lyophilized gastrin is
    made immediately before application.
L11 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2001 ACS
AN
    1974:137186 CAPLUS
DN
    80:137186
TI
    Parenterally applicable angiotensin preparation with depot action
    Matthias, Dietrich; Baumann, Hannelore; Engler, Eberhard; Wolf,
IN
    Ingrid
    Ger. (East), 2 pp.
SO
    CODEN: GEXXA8
DT
    Patent
LΑ
    German
FAN.CNT 1
    PATENT NO. KIND DATE
                                       APPLICATION NO. DATE
                   ____
                                        -----
    _____
    DD 98610
                    Z
                          19730712 DD 1972-163087
PΙ
                                                        19720515
AB
    A title prepn. is made by dissolving 2.5 mg lyophilized
    angiotensin (I) in 1.1-1.5 ml aq. 10-50% soln. of
    poly(vinylpyrrolidinone)(mol. wt. 25,000-35,000), or as tablets,
by mixing
    I with 2 g lactose or NaCl + 2% talc to yield 2.5-50 mg implants
    1.0-5.5 mg I. Both prepns. caused a rise in blood pressure of
rats.
=> d his
     (FILE 'HOME' ENTERED AT 15:53:06 ON 07 NOV 2001)
    FILE 'EMBASE, MEDLINE, BIOSIS, USPATFULL, JAPIO, WPIDS, CAPLUS,
AGRICOLA,
    LIFESCI, BIOTECHDS, JICST-EPLUS' ENTERED AT 15:53:14 ON 07 NOV
2001
              E ENGEL JURGEN/AU
L1
           222 S E3
              E WICHERT BURKHARD/AU
L2
            12 S E3-E4
              E SAUERBIER DIETER/AU
L3
            42 S E1-E3
               E REISSMAN THOMAS/AU
L4
             5 S E1-E4
L5
           261 S L1-L4
L6
            29 S L5 AND CETRORELIX
            22 DUP REM L6 (7 DUPLICATES REMOVED)
L7
              E WOLF INGRID/AU
L8
           44 S E3-E5
L9
           0 S L8 AND CETRORELIX
L10
           6 S L8 AND LYOPHILIZ?
           6 DUP REM L10 (0 DUPLICATES REMOVED)
L11
```

=> d bib 1-6

```
L12 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2001 ACS
AN
    1992:46317 CAPLUS
DN
    116:46317
TI
    Preparation of a stable parenteral immunostimulant composition
containing
    splenopentin
IN
    Wolf, Ingrid
PA
    Berlin-Chemie A.-G., Germany
SO
    Ger. (East), 3 pp.
    CODEN: GEXXA8
DT
    Patent
LA
    German
FAN.CNT 1
    PATENT NO. KIND DATE APPLICATION NO. DATE
                                       -----
    DD 292382 A5 19910801 DD 1990-338431 19900306
    DD 292382
                   B5 19940324
    EP 445581 A1 19910911
EP 445581 B1 19930505
                                      EP 1991-102431 19910220
                   B1 19930505
        R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE
    AT 88903 E 19930515 AT 1991-102431 19910220
    ES 2055469
                   T3 19940816
                                      ES 1991-102431 19910220
    CA 2037531 AA 19910907
JP 04211611 A2 19920803
JP 06092315 B4 19941116
                                      CA 1991-2037531 19910304
                                      JP 1991-38808
                                                      19910305
PRAI DD 1990-338431
                    19900306
    EP 1991-102431
                        19910220
L12 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2001 ACS
AN
    1989:463948 CAPLUS
DN
    111:63948
TI
    Sustained-release pharmaceuticals containing peptide-sulfonated
    polystyrene complexes
IN
    Fechner, Klaus; Bienert, Michael; Klauschenz, Erhard; Wolf,
    ; Mehlis, Burkhard; Loth, Fritz; Dautzenberg, Horst; Bergfeld,
Jost
PΑ
    Akademie der Wissenschaften der DDR, Ger. Dem. Rep.
SO
    Ger. (East), 4 pp.
    CODEN: GEXXA8
DT
    Patent
LA
    German
FAN.CNT 1
    PATENT NO.
                KIND DATE
                                      APPLICATION NO. DATE
    -----
                                      -----
                                                      ------
PΙ
    DD 256605
                   A3
                         19880518
                                      DD 1982-246469
                                                      19821223
```

L12 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2001 ACS

AN 1981:127390 CAPLUS

DN 94:127390

TI Lyophilized LHRH preparations

```
Wolf, Ingrid; Schneider, Anita; Tschauschev, Peter
IN
PA
    Ger. Dem. Rep.
SO
    Ger. (East), 5 pp.
    CODEN: GEXXA8
DT
    Patent
LΑ
    German
FAN.CNT 1
    PATENT NO. KIND DATE
                                    APPLICATION NO. DATE
    -----
                                    -----
    DD 141996
PΙ
                 \boldsymbol{z}
                       19800604
                                    DD 1979-211139 19790221
L12 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2001 ACS
AN
    1980:169260 CAPLUS
DN
    92:169260
TI
    Lyophilicized hypotensive preparation for parenteral application
    Wolf, Ingrid; Klehr, Gabriele
IN
PA
    Ger. Dem. Rep.
    Ger. (East), 6 pp.
SO
    CODEN: GEXXA8
DT
    Patent
LA
    German
FAN.CNT 1
    PATENT NO. KIND DATE APPLICATION NO. DATE
                                                   -----
    DD 138406 Z 19791031
                                    DD 1978-207389 19780821
PΙ
    DD 138406
                   B1 19860507
L12 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2001 ACS
AN
    1975:484842 CAPLUS
DN 83:84842
TI
    Lyophilized gastrin preparations
    Wolf, Ingrid
IN
PA
    E. Ger.
SO
    Ger. (East), 6 pp.
    CODEN: GEXXA8
DT
    Patent
LΑ
    German
FAN.CNT 1
    PATENT NO. KIND DATE APPLICATION NO. DATE
                                     ______
    DD 109512
                    Z
                        19741112 DD 1974-176286
ΡI
                                                    19740131
L12 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2001 ACS
AN
    1974:137186 CAPLUS
DN
    80:137186
ΤI
    Parenterally applicable angiotensin preparation with depot action
    Matthias, Dietrich; Baumann, Hannelore; Engler, Eberhard; Wolf,
IN
    Ingrid
SO
    Ger. (East), 2 pp.
    CODEN: GEXXA8
DT
    Patent
LA
    German
FAN.CNT 1
    PATENT NO. KIND DATE
    DD 98610 – DATE
                                    APPLICATION NO. DATE
                                     ______
                 Z 19730712 DD 1972-163087 19720515
```

DD 98610

PΙ

The following are valid formats:

```
ABS ----- GI and AB
ALL ----- BIB, AB, IND, RE
APPS ----- AI, PRAI
BIB ----- AN, plus Bibliographic Data and PI table (default)
CAN ----- List of CA abstract numbers without answer numbers
CBIB ----- AN, plus Compressed Bibliographic Data
DALL ----- ALL, delimited (end of each field identified)
DMAX ----- MAX, delimited for post-processing
FAM ----- AN, PI and PRAI in table, plus Patent Family data
FBIB ----- AN, BIB, plus Patent FAM
IND ----- Indexing data
IPC ----- International Patent Classifications
MAX ----- ALL, plus Patent FAM, RE
PATS ----- PI, SO
SAM ----- CC, SX, TI, ST, IT
SCAN ----- CC, SX, TI, ST, IT (random display, no answer numbers;
             SCAN must be entered on the same line as the DISPLAY,
             e.g., D SCAN or DISPLAY SCAN)
STD ----- BIB, IPC, and NCL
IABS ----- ABS, indented with text labels
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
IMAX ----- MAX, indented with text labels
ISTD ----- STD, indented with text labels
OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels
SBIB ----- BIB, no citations
SIBIB ----- IBIB, no citations
HIT ----- Fields containing hit terms
HITIND ----- IC, ICA, ICI, NCL, CC and index field (ST and IT)
             containing hit terms
HITRN ----- HIT RN and its text modification
HITSTR ----- HIT RN, its text modification, its CA index name, and
             its structure diagram
FHITSTR ---- First HIT RN, its text modification, its CA index name,
and
             its structure diagram
KWIC ----- Hit term plus 20 words on either side
OCC ----- Number of occurrence of hit term and field in which it
occurs
```

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, KWIC, and OCC) may be used with DISPLAY ACC to view a

specified Accession Number. ENTER DISPLAY FORMAT (BIB):.

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L12 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2001 ACS
     1981:127390 CAPLUS
AN
DN
    94:127390
TI Lyophilized LHRH preparations
     Wolf, Ingrid; Schneider, Anita; Tschauschev, Peter
IN
PA Ger. Dem. Rep.
     Ger. (East), 5 pp.
SO
     CODEN: GEXXA8
DT
     Patent
LΑ
     German
FAN.CNT 1
     PATENT NO. KIND DATE APPLICATION NO. DATE
     -----
                                          ______
PI DD 141996 Z 19800604
                                          DD 1979-211139 19790221
=> e schneider anita/au
                   SCHNEIDER ANGELA/AU
E1
            8
            10
E2 ·
                   SCHNEIDER ANGELIKA/AU
E3
           1 --> SCHNEIDER ANITA/AU
          3 SCHNEIDER ANITA/AU
3 SCHNEIDER ANITA M H/AU
11 SCHNEIDER ANJA/AU
8 SCHNEIDER ANKE/AU
1 SCHNEIDER ANN/AU
3 SCHNEIDER ANN T/AU
2 SCHNEIDER ANNA/AU
2 SCHNEIDER ANNA M/AU
14 SCHNEIDER ANNE/AU
5 SCHNEIDER ANNE MARIE/AU
E4
E5
E6
E7
E8
E9
E10
E11
E12
=> s e3-e4
            4 ("SCHNEIDER ANITA"/AU OR "SCHNEIDER ANITA M H"/AU)
=> d bib ab 1-4
L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2001 ACS
AN 1981:127390 CAPLUS
DN
    94:127390
TI
    Lyophilized LHRH preparations
     Wolf, Ingrid; Schneider, Anita; Tschauschev, Peter
IN
PA
     Ger. Dem. Rep.
SO
     Ger. (East), 5 pp.
     CODEN: GEXXA8
DT
     Patent
LA
    German
FAN.CNT 1
     PATENT NO. KIND DATE
                                          APPLICATION NO. DATE
                           -----
     -----
                                           -----
                      Z 19800604
    DD 141996
ΡI
                                          DD 1979-211139 19790221
AB
    A stable LH-RH [9034-40-6] prepn. is made by buffering an ag.
soln. of
     LH-RH to pH 3.5-6.5 and lyophilizing. For example, 4.5 g LH-RH,
to 2 q
```

citric acid [77-92-9] and 20 g mannitol (carrier) were dissolved in 900 mL H2O for injection, dild. to 1 L, and adjusted to pH 3.5-4.5 with 1N

NaOH. The soln. was sterilized by filtration, divided into 1 mL aliquots,

and lyophilized.

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2001 ACS

AN 1975:507670 CAPLUS

DN 83:107670

TI Standardization of potassium permanganate solutions by titration with

sodium oxalate in the presence of perchloric acid and  $\mbox{\tt manganese}\left(\mbox{\tt II}\right)$ 

sulfate

AU Ohlweiler, Otto A.; Schneider, Anita M. H.

CS Inst. Quim., Univ. Fed. Rio Grande Sul, Porto Alegre, Brazil

SO An. Assoc. Bras. Quim. (1972), 28(1-2), 23-9 CODEN: AABQAL

DT Journal

LA Portuguese

AB Substituting HClO4 for H2SO4 in the standardization of 0.1N KMnO4 by

direct titrn. of Na2C2O4 in the presence of MnSO4 permits the titrn. at  $\,$ 

any temp. between 25.degree. and 80.degree.. The HClO4 concn. is maintained >2N. The KMnO4 soln. can be added at rates .ltoreq.12 ml/min.

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2001 ACS

AN 1972:121112 CAPLUS

DN 76:121112

TI Standardization of potassium permanganate by titration of sodium oxalate

in presence of perchloric acid and manganese(II) sulfate

AU Ohlweiler, O. A.; Schneider, Anita M. H.

CS Inst. Quim., Univ. Fed., Porto Alegre, Brazil

SO Anal. Chim. Acta (1972), 58(2), 477-80 CODEN: ACACAM

DT Journal

LA English

AB KMnO4 (0.1 N) was standardized with 0.24 or 0.26 parts/103 std. deviation

by titrating 0.08-0.09N Na2C2O4, in the presence of HClO4 and MnSO4

catalyst, with the KMnO4 soln. at 25.degree. or 60.degree., resp.

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2001 ACS

AN 1970:50566 CAPLUS

DN 72:50566

TI Colorimetric determination of cobalt with phthalocyanine

AU Meditsch, Jorge de Oliveira; Schneider, Anita M. H.

CS Univ. Rio Grande do Sul, Rio Grande do Sul, Brazil

SO Rev. Quim. Ind. (Rio de Janeiro) (1969), 38(446), 16-18 CODEN: RQIRAI

DT Journal

LA Portuguese

AB Heat 200 mg of flux (phthalic anhydride 14.8, urea 6, and boric acid 0.1 g

) with the Co++ soln. at 160-5.degree.C for 5 min and ext. the Co complex form ed with acetone. After making up to vol. measure the absorbance at 622 m.mu. Co++ can be detd. in the 2.5-20 ppm range. The av. relative error is 5%. Fe++ and Cu++ interfere, .ltoreg.100 ppm of Ni++ can be tolerated, while Ca++, Ba++, Sr++, Mg++, Zn++, Cd++, Hg++, and Mn++ do not interfere. => e tschauschev peter/au E1 1 TSCHAUSCHE S J/AU TSCHAUSCHEV P/AU E2 14 E3 4 --> TSCHAUSCHEV PETER/AU E4 1 TSCHAUSHEV G/AU E5 1 TSCHAUSHEV P/AU E6 4 TSCHAUT R J/AU E7 3 TSCHAUTSCHEV P/AU E8 3 TSCHAWDAROVA R/AU E9 2 TSCHAWDAROWA M/AU E10 2 TSCHAWOW A/AU 1 E11 TSCHAWOW ANTOANETA/AU E12 4 TSCHAWRAKOW G/AU => s e2-e520 ("TSCHAUSCHEV P"/AU OR "TSCHAUSCHEV PETER"/AU OR L14"TSCHAUSHEV G"/AU OR "TSCHAUSHEV P"/AU) => s l14 and lyophili? L15 1 L14 AND LYOPHILI? => d bib ab ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS L15 AN1981:127390 CAPLUS DN 94:127390 TILyophilized LHRH preparations Wolf, Ingrid; Schneider, Anita; Tschauschev, Peter IN PΑ Ger. Dem. Rep. Ger. (East), 5 pp. SO CODEN: GEXXA8 DT Patent LΑ German FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----------ΡI DD 141996 Z DD 1979-211139 19800604 19790221

A stable LH-RH [9034-40-6] prepn. is made by buffering an aq. AΒ LH-RH to pH 3.5-6.5 and lyophilizing. For example, 4.5 g LH-RH,

to 2 g citric acid [77-92-9] and 20 g mannitol (carrier) were dissolved

in 900 mL H2O for injection, dild. to 1 L, and adjusted to pH 3.5-4.5 with 1N NaOH. The soln. was sterilized by filtration, divided into 1 mLaliquots, and lyophilized. => s cetrorelix and lyophili? L16 22 CETRORELIX AND LYOPHILI? => dup rem 116 PROCESSING COMPLETED FOR L16 19 DUP REM L16 (3 DUPLICATES REMOVED) L17 => d bib ab 1-19 L17 ANSWER 1 OF 19 USPATFULL DUPLICATE 1 AN 2001:14464 USPATFULL ΤI Pharmaceutical formulations for sustained drug delivery Gefter, Malcolm L., Lincoln, MA, United States INBarker, Nicholas, Southborough, MA, United States Musso, Gary, Hopkinton, MA, United States Molineaux, Christopher J., Brookline, MA, United States PΑ Praecis Pharmaceuticals, Inc., Cambridge, MA, United States (U.S. corporation) PΙ US 6180608 B1 20010130 ΑI US 1997-988851 19971211 (8) RLI Continuation-in-part of Ser. No. US 1996-762747, filed on 11 Dec 1996, now patented, Pat. No. US 5968895 DT Utility Granted FS EXNAM Primary Examiner: Cintins, Marianne M.; Assistant Examiner: Delacroix-Muirheid, C. LREP Lahive & Cockfield, LLP, DeConti, Jr., Giulio A., Laccotripe, Maria C. CLMN Number of Claims: 50 ECL Exemplary Claim: 1 DRWN 8 Drawing Figure(s); 5 Drawing Page(s) LN.CNT 1333 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Sustained delivery formulations comprising a water-insoluble complex of a peptidic compound (e.g., a peptide, polypeptide, protein, peptidomimetic or the like) and a carrier macromolecule are disclosed. The formulations of the invention allow for loading of high concentrations of peptidic compound in a small volume and for delivery of a pharmaceutically active peptidic compound for prolonged periods, e.g., one month, after administration of the complex. The

the invention can be milled or crushed to a fine powder. In

complexes of

powdered

form, the complexes form stable aqueous suspensions and dispersions,

suitable for injection. In a preferred embodiment, the peptidic compound

of the complex is an LHRH analogue, preferably an LHRH antagonist, and

the carrier macromolecule is an anionic polymer, preferably carboxymethylcellulose. Methods of making the complexes of the invention, and methods of using LHRH-analogue-containing complexes to

treat conditions treatable with an LHRH analogue, are also disclosed.

L17 ANSWER 2 OF 19 USPATFULL

AN 2001:144937 USPATFULL

TI Solid matrix therapeutic compositions

IN Unger, Evan C., Tucson, AZ, United States

PA ImaRx Therapeutics, Inc. (U.S. corporation)

PI US 2001018072 A1 20010830

AI US 2001-828762 A1 20010409 (9)

RLI Division of Ser. No. US 1998-75477, filed on 11 May 1998, PENDING

PRAI US 1997-46379 19970513 (60)

DT Utility

FS APPLICATION

LREP Mackiewicz & Norris LLP, One Liberty Place - 46th Floor, Philadelphia,

PA, 19103

CLMN Number of Claims: 38

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 4899

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a solid porous matrix comprising a

surfactant in combination with a bioactive agent. The solid porous

matrix may be prepared by combining a surfactant and a therapeutic,

together with a solvent, to form an emulsion containing random aggregates of the surfactant and the therapeutic, and processing the

emulsion by controlled drying, or controlled agitation and controlled

drying to form the solid porous matrix.

L17 ANSWER 3 OF 19 USPATFULL

AN 2001:90106 USPATFULL

TI Methods for detecting lesions in dense breast tissue using LHRH antagonists

IN Garnick, Marc B., Brookline, MA, United States

PA Praecis Pharmaceuticals Incorporated (U.S. corporation)

PI US 2001002249 A1 20010531

AI US 2001-764626 A1 20010118 (9)

RLI Continuation of Ser. No. US 1998-67327, filed on 27 Apr 1998, GRANTED,

Pat. No. US 6217844

DT Utility

FS APPLICATION

```
LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
LREP
CLMN
       Number of Claims: 31
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 687
       Improved methods for detecting lesions in dense breast tissue
AΒ
are
       disclosed. The methods of the invention generally feature
administration
       to a subject of an LHRH antagonist in an amount and for a
period of time
       sufficient to reduce the density of breast tissue prior to
generating an
       image of the breast tissue, for example by mammography, to
       lesion in the breast tissue. Packaged formulations for
reducing breast
       density in a subject prior to generating an image of the
       breast tissue, comprising an LHRH antagonist packaged with
instructions
       for using the LHRH antagonist to reduce breast density in a
subject
       prior to imaging the breast tissue, are also disclosed.
L17
    ANSWER 4 OF 19 USPATFULL
AN
       2001:121065 USPATFULL
TI
       Attaching agents to tissue with transglutaminase and a
transglutaminase
       substrate
       Green, Howard, 82 Williston St., Brookline, MA, United States
IN
02146
       Corey, George D., 65 Harding St., Newton, MA, United States
02165
       Compton, Bruce J., 30 Cottage St., Lexington, MA, United
States 02173
      Dijan, Philippe, 170, rue de la Convention, 75015 Paris, France
PΙ
      US 6267957
                        B1
                               20010731
ΑI
      US 1999-234358
                               19990120 (9)
      US 1998-71908
PRAI
                           19980120 (60)
DT
      Utility
FS
      GRANTED
EXNAM Primary Examiner: Naff, David M.
LREP
      Wolf, Greenfield & Sacks, P.C.
CLMN
      Number of Claims: 48
      Exemplary Claim: 1
ECL
DRWN
       3 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1730
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       Methods, products and kits are provided for attaching agents
to tissue
       with a linking molecule in the presence of transglutaminase.
The linking
      molecule and/or agent is a substrate of transglutaminase. The
agent can
      be a nonprotein or an enzyme such as cholinesterase or
      phosphodiesterase. The transglutaminase may be exogenously
added or be
       endogenous in tissue. In specific embodiments, the linking
molecule
```

contains at least two contiguous linked glutamines or at least three

contiguous linked lysines. A conjugate of the agent and the linking

molecule may be applied to tissue, and in the presence of transglutaminase covalently bonded to the tissue via the linking

molecule. A complementary linking molecule rich in lysines may be first

attached to the tissue in the presence of transglutaminase, and then

covalently bonded to a glutamine-containing linking molecule of the

conjugate in the presence of transglutaminase. In another embodiment, a

linking molecule containing multiple glutamines is covalently bonded to

tissue in the presence of transglutaminase, and an agent containing

multiple lysines is covalently bonded to the linking molecule in the

presence of transglutaminase. Alternatively, the linking molecule

contains multiple lysines and the agent contains multiple glutamines.

Two tissues can be sealed together by holding the tissues in contact

with each other in the presence of transglutaminase.

L17 ANSWER 5 OF 19 USPATFULL

AN 2001:108015 USPATFULL

TI Process for the one-stage resulting and purification of oligopeptides

IN Gunther, Kurt, Staatsangehorigkeit, Germany, Federal Republic of

Kunz, Franz-Rudolf, Staatsangehorigkeit, Germany, Federal Republic of

Drauz, Karlheinz, Staatsangehorigkeit, Germany, Federal Republic of

Muller, Thomas, Staatsangehorigkeit, Germany, Federal Republic of

PA Degussa-Huls Aktiengesellschaft, Germany, Federal Republic of (non-U.S.

corporation)

PI US 6258933 B1 20010710

AI US 1999-276709 19990326 (9)

PRAI DE 1998-19813849 19980327

DT Utility

FS GRANTED

EXNAM Primary Examiner: Low, Christopher S. F.

LREP Pillsbury Madison & Sutro LLP

CLMN Number of Claims: 16

ECL Exemplary Claim: 1

DRWN 9 Drawing Figure(s); 5 Drawing Page(s)

LN.CNT 507

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a process for the one-stage resalting

and purification of oligopeptides. Oligopeptides are often not formed

directly as acetates when synthesised. Acetate salts of oligopeptides

are however desirable as bulk-active material for medical and formulation reasons. Processes known from the prior art have hitherto

involved two separate steps or pyridine-containing solvents. The

resalting and purification can be combined in one step and the use of

 $% \left( 1\right) =\left( 1\right) +\left( 1\right) +\left($ 

its chloride salt is purified with an acetate-containing solvent by

liquid chromatography methods.

L17 ANSWER 6 OF 19 USPATFULL

AN 2001:55422 USPATFULL

TI Methods for detecting lesions in dense breast tissue using LHRH antagonists

IN Garnick, Marc B., Brookline, MA, United States

PA Praecis Pharmaceuticals, Inc., Cambridge, MA, United States (U.S.

corporation)

PI US 6217844 B1 20010417 AI US 1998-67327 19980427 (9)

DT Utility FS Granted

EXNAM Primary Examiner: Jones, Dameron

LREP Lahive & Cockfield, LLP, DeConti, Jr., Giulio A., Laccotripe, Maria C.

CLMN Number of Claims: 22 ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 768

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Improved methods for detecting lesions in dense breast tissue are

disclosed. The methods of the invention generally feature administration

to a subject of an LHRH antagonist in an amount and for a period of time

sufficient to reduce the density of breast tissue prior to generating an

image of the breast tissue, for example by mammography, to detect a

lesion in the breast tissue. Packaged formulations for reducing breast

density in a subject prior to generating an image of the subject's

breast tissue, comprising an LHRH antagonist packaged with instructions

for using the LHRH antagonist to reduce breast density in a subject

prior to imaging the breast tissue, are also disclosed.

L17 ANSWER 7 OF 19 USPATFULL

AN 2001:52022 USPATFULL

TI GnRH antagonists being modified in positions 5 and 6

IN Semple, Graeme, Gothenburg, Sweden

```
Jiang, Guangcheng, San Diego, CA, United States
       Ferring BV, Hoofddorp, Netherlands (non-U.S. corporation)
PA
ΡI
       US 6214798
                          B1
                               20010410
       WO 9846634 19981022
ΑI
       US 2000-402698
                               20000103 (9)
       WO 1998-US7438
                               19980413
                               20000103 PCT 371 date
                               20000103 PCT 102(e) date
RLI
       Continuation-in-part of Ser. No. US 1997-837042, filed on 11
Apr 1997,
       now patented, Pat. No. US 5925730
DT
       Utility
       Granted
FS
EXNAM
      Primary Examiner: Jones, Dwayne C.; Assistant Examiner:
       Delacroix-Muirheid, C.
       Fitch, Even, Tabin & Flannery
LREP
CLMN
       Number of Claims: 20
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 1463
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Peptides are provided which have improved duration of GnRH
antagonistic
       properties. These antagonists may be used to regulate
fertility and to
       treat steroid-dependent tumors and for other short-term and
long-term
       treatment indications. These antagonists have a derivative of
aminoPhe
       or its equivalent in the 5- or the 5- and 6-positions. This
derivative
       is modified so as to contain a carbamoyl group or heterocycle,
including
       a urea moiety, in its side chain. Decapeptides having the
formula:
Ac-D-2Nal-D-4Cpa-D-3Pal-Ser-4Aph(L-hydroorotyl)-D-4Amf(Q.sub.2)-Leu-
       Lys(isopropyl)-Pro-Xaa.sub.10,
       wherein Q.sub.2 is Cbm or MeCbm and Xaa.sub.10 is D-Ala-ol or
Ala-ol are
       particularly effective and continue to exhibit very substantial
       suppression of LH secretion at 96 hours following injection.
L17
    ANSWER 8 OF 19 CAPLUS COPYRIGHT 2001 ACS
     2001:764638 CAPLUS
AN
     Low-temperature micronization of a peptide drug in fluid
TI
propellant: case
     study cetrorelix
    Lizio, Rosario; Damm, Michael; Sarlikiotis, Antonio W.; Bauer,
ΑU
Horst H.;
     Lehr, Claus-Michael
    Dep. Biopharmaceutics and Pharmaceutical Technol., Saarland
CS
Univ.,
    Saarbrucken, 66123, Germany
SO
    AAPS PharmSciTech (2001), 2(3), No pp. given
    CODEN: AAPHFZ; ISSN: 1522-1059
    URL:
http://www.aapspharmaceutica.com/scientificjournals/volume2issue3/049
```

/manuscript.pdf

- PB American Association of Pharmaceutical Scientists
- DT Journal; (online computer file)
- LA English
- AB Aim of this study was to elaborate an efficient method for the micronization of the decapeptide cetrorelix (a GnRH-antagonist), in order to obtain a microsuspension as basis for other pharmaceutical
- prepns., such as e.g. inhalation aerosols. A modified pearl-mill coupled
- with a cryostat was used for the micronization of cetrorelix in fluid propellant and operated under different conditions. The obtained
- cetrorelix suspensions were analyzed for particle size
   distribution, purity of cetrorelix, and for metal contamination
   through abrasion from parts of the mill. The method allowed an
  effective
  - micronization of cetrorelix. The mean particle size of the initial cetrorelix lyophilizate bulk were was reduced
- from 52.5 .mu.m (Vol. Mean Diam., VMD) down to 14.9, 6.1 and 3.1 .mu.m,
- resp., resp. The HPLC anal. of all cetrorelix suspensions after micronization did not show signs of decompn. as compared to the initial
- product. The elementary anal. of the suspensions performed by inductively
- coupled plasma mass spectrometry revealed a negligible amt. of contaminants in the suspension (Zr = max. 0.6 ppm; Fe, Cr, Ni, Ba, below
- limit of quantification, i.e. < 0.14 ppm). The only appreciable
   contaminant, Aluminum (Al = 1.1 ppm), was derived from the mech.
  capping</pre>
- of aluminum canisters prior to anal. The Zr detn. in the suspension of
- 0.6 ppm, is still considered to be negligible as compared to the legally  $\ensuremath{\text{legally}}$
- tolerated limit of air contamination. By low-temp. micronization in fluid
- propellant, fine drug suspensions of **cetrorelix** for pMDIs can be directly manufd. in one-step procedure without destruction of the peptide
  - structure and without appreciable product contamination.
- L17 ANSWER 9 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
- AN 2000:477618 BIOSIS
- DN PREV200000477618
- TI Process for the preparation of immobilized and activity-stabilized
  - complexes of LHRH antagonists.
- AU Engel, Jurgen (1); Deger, Wolfgang; Reissmann, Thomas; Losse, Gunter;
  - Naumann, Wolfgang; Murgas, Sandra
- CS (1) Alzenau Germany
  - ASSIGNEE: Asta Medica Aktiengesellschaft, Dresden, Germany
- PI US 6054555 April 25, 2000
- SO Official Gazette of the United States Patent and Trademark Office Patents,
  - (Apr. 25, 2000) Vol. 1233, No. 4, pp. No pagination. e-file. ISSN: 0098-1133.

DT Patent

LA English

AB In this invention, a release-delaying system is to be developed for LHRH

antagonists, in particular for **cetrorelix**, which allows the active compound to be released in a controlled manner over several weeks

by complexation with suitable biophilic carriers. The acidic polyamino

acids polyglutamic acid and polyaspartic acid were selected for complexation with cetrorelix. The cetrorelix polyamino

acid complexes are prepared from aqueous solutions by combination of the

solutions and precipitation of the complexes, which are subsequently

centrifuged off and dried over P2 O5 in vacuo. If complexes having a

defined composition are to be obtained, lyophilization proves to be a suitable method. The cetrorelix-carboxylic acid complexes were also prepared from the aqueous solutions. In the random liberation

system, the acidic polyamino acids poly-Glu and poly-Asp showed good

release-delaying properties as a function of the hydrophobicity and the

molecular mass of the polyamino acid. In animal experiments, it was

possible to confirm the activity of the **cetrorelix**-polyamino acid complexes as a depot system in principle. It is thus possible by

complexation of **cetrorelix** with polyamino acids to achieve testosterone suppression in male rats over 600 hours. The release of

active compound here can be controlled by the nature and the molecular

mass of the polymers.

L17 ANSWER 10 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3

AN 2000:355483 BIOSIS

DN PREV200000355483

TI Immobilized and activity-stabilized complexes of LHRH antagonists and

processes for their preparation.

AU Engel, Jurgen (1); Deger, Wolfgang; Reissmann, Thomas; Losse, Gunter;

Naumann, Wolfgang; Murgas, Sandr

CS (1) Alzenau Germany

ASSIGNEE: Asta Medica Aktiengesellschaft, Dresden, Germany

PI US 6022860 February 08, 2000

SO Official Gazette of the United States Patent and Trademark Office Patents,

(Feb. 8, 2000) Vol. 1231, No. 2, pp. No pagination. e-file. ISSN: 0098-1133.

DT Patent

LA English

AB In this invention, a release-delaying system is to be developed for LHRH

antagonists, in particular for **cetrorelix**, which allows the active compound to be released in a controlled manner over several weeks

by complexation with suitable biophilic carriers. The acidic polyamino

acids polyglutamic acid and polyaspartic acid were selected for complexation with cetrorelix. The cetrorelix polyamino

acid complexes are prepared from aqueous solutions by combination of the

solutions and precipitation of the complexes, which are subsequently

centrifuged off and dried over P2 O5 in vacuo. If complexes having a  $\,$ 

defined composition are to be obtained, lyophilization proves to be a suitable method. The cetrorelix-carboxylic acid complexes were also prepared from the aqueous solutions. In the random liberation

system, the acidic polyamino acids poly-Glu and poly-Asp showed good

release-delaying properties as a function of the hydrophobicity and the  $\,$ 

molecular mass of the polyamino acid. In animal experiments, it was

possible to confirm the activity of the **cetrorelix**-polyamino acid complexes as a depot system in principle. It is thus possible by

complexation of **cetrorelix** with polyamino acids to achieve testosterone suppression in male rats over 600 hours. The release of

active compound here can be controlled by the nature and the molecular

mass of the polymers.

L17 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2001 ACS

AN 2000:573692 CAPLUS

DN 133:182987

TI Sustained release salts of pharmaceutically active peptides and their

production

IN Bauer, Horst; Deger, Wolfgang; Sarlikiotis, Werner; Damm, Michael

PA Asta Medica A.-G., Germany

SO PCT Int. Appl., 23 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2000047234 A1 20000817 WO 2000-EP697 20000129 W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN,

IS, JP,

KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI,

SK, TR,

UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL,

PT, SE

PRAI US 1999-119076 P 19990208

AB Substained delivery pharmaceutical compns. comprise a water insol. salt of

a pharmaceutically active ionic peptide and a counterionic carrier

macromol. The peptide may be an LHRH antagonist such as cetrorelix and the macromol. may be an anionic polysaccharide such as CM-cellulose. The salt is prepd. using ion exchangers to sep. remove the counterions from the peptide and the carrier macromol. thereby forming free peptide/macromol. ions. These free peptide and macromol. ions are then combined to form the water insol. peptide-macromol. salt. A lyophilizate of cetrorelix-CM-cellulose salt was prepd. RE.CNT 6 RE (1) Asta Medica Ag; WO 9842381 A 1998 CAPLUS (2) Kamei, S; WO 9832423 A 1998 CAPLUS (3) Klokkers-Bethke, K; US 5773032 A 1998 CAPLUS (4) Molineaux, C; WO 9825642 A 1998 CAPLUS (5) Nestor, J; US 4581169 A 1986 CAPLUS ALL CITATIONS AVAILABLE IN THE RE FORMAT L17 ANSWER 12 OF 19 USPATFULL AN1999:128511 USPATFULL ΤI Pharmaceutical formulations for sustained drug delivery IN Gefter, Malcolm L., Lincoln, MA, United States Barker, Nicholas, Southborough, MA, United States Musso, Gary, Hopkinton, MA, United States Molineaux, Christopher J., Brookline, MA, United States Praecis Pharmaceuticals, Inc., Cambridge, MA, United States PΑ (U.S. corporation) PΙ US 5968895 19991019 US 1996-762747 ΑI 19961211 (8) DTUtility FS Granted EXNAM Primary Examiner: Richter, Johann; Assistant Examiner: Delacroix-Muirheid, C. LREP Lahive & Cockfield, LLP, Mandragouras, Amy E., DeConti, Giulio Α. CLMN Number of Claims: 32 ECLExemplary Claim: 10 DRWN 2 Drawing Figure(s); 2 Drawing Page(s) LN.CNT 775 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Sustained delivery formulations comprising a water-insoluble complex of a peptide and a carrier macromolecule are disclosed. The formulations of the invention allow for loading of high concentrations of peptide in a small volume and for delivery of a pharmaceutically active peptide for prolonged periods, e.g., one month, after administration of the complex. The complexes of the invention can be milled or crushed to a fine powder. In powdered form, the complexes form stable aqueous suspensions and dispersions, suitable for injection. In a preferred

embodiment, the

peptide of the complex is an LHRH analogue, preferably an LHRH antagonist, and the carrier macromolecule is an anionic polymer,

preferably carboxymethylcellulose. Methods of making the complexes of

the invention, and methods of using LHRH-analogue-containing complexes

to treat conditions treatable with an LHRH analogue, are also disclosed.

L17 ANSWER 13 OF 19 USPATFULL

AN 1999:99641 USPATFULL

TI LH-RH antagonists having improved action

IN Kutscher, Bernhard, Maintal, Germany, Federal Republic of Bernd, Michael, Frankfurt, Germany, Federal Republic of Beckers, Thomas, Frankfurt, Germany, Federal Republic of Klenner, Thomas, Ingelheim, Germany, Federal Republic of Emig, Peter-Paul, Bruchkobel, Germany, Federal Republic of Charpentier, Patricia-Marie, Maintal, Germany, Federal

Republic of

PA ASTA Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of

(non-U.S. corporation)

PI US 5942493 19990824 AI US 1998-87274 19980528 (9)

RLI Continuation-in-part of Ser. No. WO 1996-DE2171, filed on 14 Nov 1996

PRAI DE 1995-19544212 19951128

DT Utility

FS Granted

EXNAM Primary Examiner: Davenport, Avis M.

LREP Pillsbury Madison & Sutro LLP

CLMN Number of Claims: 16 ECL Exemplary Claim: 1

DRWN 6 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 1219

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB New LH-RH antagonists are disclosed, in particular peptidomimetics and

peptides modified in a side chain, their salts with pharmaceutically

acceptable acids and a process for preparing these LH-RH antagonists and

their salts. The disclosed peptides represent analogues of the luteinising hormone releasing hormone (LH-RH). The disclosed compounds

have a high antagonistic power and are free of undesirable side effects,

in particular edematogenic effects.

L17 ANSWER 14 OF 19 USPATFULL

AN 1999:81921 USPATFULL

TI GnRH antagonists

IN Semple, Graeme, Hampshire, United Kingdom Jiang, Guangcheng, San Diego, CA, United States

PA Ferring BV, Hoofddorp, Netherlands (non-U.S. corporation)

PI US 5925730 19990720 AI US 1997-837042 19970411 (8)

DT Utility

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FS
       Granted
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner:
       Delacroix-Muirheid, C.
       Fitch, Even, Tabin & Flannery
LREP
CLMN
       Number of Claims: 21
       Exemplary Claim: 1
ECL
DRWN
      No Drawings
LN.CNT 1458
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Peptides are provided which have improved duration of GnRH
antagonistic
       properties. These antagonists may be used to regulate
fertility and to
       treat steroid-dependent tumors and for other short-term and
long-term
       treatment indications. These antagonists have a derivative of
aminoPhe
       or its equivalent in the 5- and/or 6-positions. This
derivative contains
       a carbamoyl group or a heterocycle including a urea in its
side chain.
       Particularly effective decapeptides, which continue to exhibit
very
       substantial suppression of LH secretion at 96 hours following
injection,
       have the formulae:
Ac-D-2Nal-D-4Cpa-D-3Pal-Ser-4Aph (hydroorotyl) -D-
       4Aph(acetyl)-Leu-Lys(isopropyl)-Pro-D-Ala-NH.sub.2, and
Ac-D-2Nal-D-4Cpa-D-3Pal-Ser-4Aph (hydroorotyl) -D-4Amf (Q.sub.2) -Leu-
       Lys(isopropyl)-Pro-D-Ala-NH.sub.2, wherein Q.sub.2 is Cbm or
MeCbm.
L17 ANSWER 15 OF 19 USPATFULL
AN
       1998:124554 USPATFULL
ΤI
       GnRH antagonist decapeptides
       Jiang, Guangcheng, San Diego, CA, United States
IN
       Semple, Graeme, Hamphire, United Kingdom
PA
       Ferring BV, Hoofddorp, Netherlands (non-U.S. corporation)
PΙ
       US 5821230
                               19981013
      US 1997-837041
ΑI
                               19970411 (8)
DT
      Utility
FS
       Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Wang,
Cecilia
       F.
LREP
     Fitch, Even, Tabin & Flannery
      Number of Claims: 20
ECL
      Exemplary Claim: 1
DRWN
      No Drawings
LN.CNT 1630
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
   Peptides are provided which have improved duration of GnRH
antagonistic
      properties and/or which can be synthesized more economically.
These
       antagonists may be used in the same manner as the compounds of
which
       they are analogs to regulate fertility and to treat
steroid-dependent
```

tumors and for other short-term and long-term treatment indications. One particularly effective peptide, a decapeptide analog of the GnRH antagonist Acyline, has the formula: Ac-D-2Nal-D-4Cpa-D-Dpr(methylcarbamoyl) -Ser-4Aph(acetyl) -D-4Aph(acetyl) -Leu-Lys(isopropyl Pro-D-Ala-NH.sub.2. It continues to exhibit very substantial suppression of LH secretion at 96 hours following injection. Other economically attractive and pharmacologically effective analogs have the formulas: Ac-D-2Nal-D-4Cpa-Xaa.sub.3 -Ser-4Aph (acetyl) -D-4Aph (acetyl) -Leu-Lys(isopropyl)-Pro-D-Ala-NH.sub.2; and Ac-D-2Nal-D-4Cpa-Xaa.sub.3 -Ser-4Aph (hydroorotyl) -D-4Aph (acetyl) -Leu-Lys (isopropyl) -Pro-D-Ala-NH.sub.2, wherein Xaa.sub.3 is D-Gln or Gln. L17 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2001 ACS 1998:672495 CAPLUS ANDN129:293891 ΤI Immobilized activity-stabilized LHRH antagonist complexes and their production Engel, Juergen; Deger, Wolfgang; Reissmann, Thomas; Losse, ΙN Naumann, Wolfgang; Murgas, Sandra PAAsta Medica Aktiengesellschaft, Germany SO PCT Int. Appl., 22 pp. CODEN: PIXXD2 DTPatent LА German FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE -----WO 9842381 Al 19981001 WO 1998-EP1398 PΙ 19980311 W: AU, BR, CA, CN, CZ, HU, IL, JP, MX, NO, NZ, PL, RU, SK, TR, UA RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE DE 19712718 A1 19981001 DE 1997-19712718 19970326 DE 19712718 C2 19990923 AU 9869207 **A**1 19981020 AU 1998-69207 19980311 A Al BR 1998-7887 BR 9807887 20000222 19980311 20000301 EP 1998-914877 19980311 EP 981377 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI T2 JP 2001520662 US 1998-48244 19980320 1998-4665 19990924 20011030 JP 1998-544811 US 6022860 A 20000208
NO 9904665 A 19990924
US 6054555 A 20000425
PRAI DE 1997-19712718 A 19970326
WO 1998-EP1398 W 19980311
US 1998-48244 A3 19980326 NO 1999-4665 US 1999-422990 19991022

AB LHRH antagonists, esp. cetrorelix, are complexed with suitable biophilic carriers to enable sustained, targeted release of the active

substance over a period of several weeks. The acidic polyamino acids,

polyaspartic and polyglutamic acids, are selected for complexation with

cetrorelix. The cetrorelix/polyamino acid complexes are produced from aq. solns. by combining the solns. and pptg. the complexes

which are subsequently centrifuged off and vacuum dried over P2O5,

preferably by lyophilization. These acidic polyamino acids display good sustained-release properties in a static liberation system

depending on the hydrophobicity and molar mass of the polyamino acids.

Animal testing demonstrated the efficacy of the **cetrorelix** /polyamino acid complexes as a depot system. By complexation of **cetrorelix** with polyamino acids, testosterone suppression can be achieved in male rats over a period of 600 h. Active substance ase

can thus be controlled according to polymer type and molar mass.

L17 ANSWER 17 OF 19 USPATFULL

AN 97:78416 USPATFULL

TI Products for administering an initial high dose of **Cetrorelix** and producing a combination package for use when treating diseases

IN Engel, Jurgen, Alzenau, Germany, Federal Republic of Hilgard, Peter, Frankfurt, Germany, Federal Republic of Reissmann, Thomas, Frankfurt, Germany, Federal Republic of

PA ASTA Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of

(non-U.S. corporation)

PI US 5663145 19970902

AI US 1994-354838 19941208 (8)

PRAI DE 1993-4342091 19931209

DT Utility

FS Granted

EXNAM Primary Examiner: Russel, Jeffrey E.

LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP

CLMN Number of Claims: 25

ECL Exemplary Claim: 7

DRWN No Drawings

LN.CNT 227

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB For application during the treatment of benign and malign tumour

diseases, the product according to the invention containing the initial

dose of **Cetrorelix** acetate and one or more maintenance doses of **Cetrorelix** acetate, **Cetrorelix** embonate or a slow-release form of **Cetrorelix**, is used as a combination

preparation for treatment to be administered at specific time intervals.

L17 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2001 ACS

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AN
    1995:677500 CAPLUS
DN
    123:65874
    Products for the application of high initial doses of cetrorelix
ΤI
    and preparation of a combined package for use in treating
diseases
    Engel, Juergen; Hilgard, Peter; Reissmann, Thomas
ΙN
PA
    Asta Medica A.-G., Germany
    Eur. Pat. Appl., 10 pp.
SO
    CODEN: EPXXDW
DT
    Patent
LΑ
    German
FAN.CNT 1
    PATENT NO. KIND DATE
                                      APPLICATION NO. DATE
                                       -----
    EP 657170 A1 19950614
EP 657170 B1 20000315
                                    EP 1994-118466
                                                        19941124
       R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,
NL, PT, SE
    AT 190495
                    Ē
                          20000415
                                        AT 1994-118466
                                                        19941124
    ES 2145803
CA 2137595
                   T3 20000716
AA 19950610
A 19970902
                                        ES 1994-118466
                                                        19941124
                                      CA 1994-2137595 19941208
    US 5663145
                                      US 1994-354838
                                                        19941208
    JP 07194670
                    A2 19950801 JP 1994-306475
                                                        19941209
PRAI DE 1993-4342091 A 19931209
    A pharmaceutical product, esp. suitable for treatment of
hormone-dependent
    tumors, comprises a package of containers, of which .qtoreq.1
containers
    contain an initial dose of drug and .gtoreq.1 addnl. containers
each
    contain a maintenance dose. The maintenance doses may be in
    delayed-release form. Thus, a 1-mo supply of cetrorelix
    comprised .gtoreg.1 container contg. an initial dose (1-60 mg)
    lyophilized cetrorelix acetate and .ltoreg.30 addnl.
    containers contq. a maintenance dose (0.1-10 mg) lyophilized
    cetrorelix acetate.
L17 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2001 ACS
AN
    1994:587330 CAPLUS
DN
    121:187330
TI
    Preparation of a cetrorelix lyophilized composition
IN
    Engel, Juergen; Sauerbier, Dieter; Wichert, Burkhard; Reissmann,
Thomas
PA
    Asta Medica AG, Germany
SO
    Eur. Pat. Appl., 5 pp.
    CODEN: EPXXDW
DT
    Patent
LΑ
    German
FAN.CNT 1
    PATENT NO.
                               APPLICATION NO. DATE
                    KIND DATE
                                       -----
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                    ----
    EP 611572 A2 19940824
PΙ
                                       EP 1994-101672 19940204
    EP 611572
EP 611572
                   A3
B1
                          19950111
                          20000607
       R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,
NL, PT, SE
    DE 4305225
                    A1
                          19940825
                                       DE 1993-4305225 19930219
    TW 387812
                    B 20000421
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A2 19991006

EP 947200

TW 1994-83100769 19940131

EP 1999-102340 19940204

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT, IE
                                          AT 1994-101672
    AT 193653
                      E
                           20000615
                                                          19940204
                           20001016
                                          ES 1994-101672
                                                          19940204
    ES 2148247
                      Т3
    CZ 284314
                      В6
                           19981014
                                          CZ 1994-312
                                                          19940214
    CZ 285768
                      В6
                           19991117
                                          CZ 1998-974
                                                          19940214
                                         AU 1994-55235
                                                          19940217
    AU 9455235
                      A1
                           19940825
    AU 671881
                     В2
                           19960912
    JP 06271476
                     A2
                           19940927
                                         JP 1994-20532
                                                          19940217
    PL 177177
                                          PL 1994-302266
                                                          19940217
                     В1
                           19991029
    CA 2115943
                      AA
                           19940820
                                          CA 1994-2115943
                                                          19940218
                                          FI 1994-779
    FI 9400779
                     Α
                           19940820
                                                          19940218
    NO 9400564
                     Α
                           19940822
                                         NO 1994-564
                                                          19940218
                                          ZA 1994-1136
    ZA 9401136
                     Α
                           19940829
                                                          19940218
    BR 9400617
                      A
                           19940927
                                          BR 1994-617
                                                          19940218
    HU 67117
                                         HU 1994-481
                     A2
                           19950228
                                                          19940218
    HU 218281
                     В
                           20000728
    CN 1112019
                                         CN 1994-101378
                                                          19940218
                      Α
                           19951122
    RU 2145234
                      C1
                           20000210
                                          RU 1994-5001
                                                          19940218
PRAI DE 1993-4305225
                           19930219
                      Α
                      A3
    EP 1994-101672
                           19940204
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AB A lyophilizate of a peptide with 3-15 amino acid residues (e.g. cetrorelix) and .gtoreq.1 optional matrix materials (e.g. mannitol) is prepd. by dissolving in 100-10,000 wt. parts AcOH, dilg. with

water, and lyophilizing the resulting soln. The
lyophilizate is useful for prepn. of a medication for treatment
of

female infertility and protection of the gonads from the follicular

hyperstimulation seen with other infertility treatments.